

Israeli R.S., Powell C.T., Fair W.R., Heston W.D.W.;  
RT "Molecular cloning of a complementary DNA encoding a prostate-specific  
RT membrane antigen.;"  
RL *Cancer Res.* 53:227-230(1993).  
RN [2]  
RP NUCLEOTIDE SEQUENCE [mRNA] (ISOFORM PSMA').  
RC TISSUE-Prostate;  
RX MEDLINE-95188188; PubMed-7882349;  
RA Su S.L., Huang I.-P., Fair W.R., Powell C.T., Heston W.D.W.;  
RT "Alternatively spliced variants of prostate-specific membrane antigen  
RT RNA: ratio of expression as a potential measurement of progression.";  
RL *Cancer Res.* 55:1441-1443(1995).  
RN [3]  
RP NUCLEOTIDE SEQUENCE [mRNA] (ISOFORMS PSMA-1 AND PSMA-2).  
RC TISSUE=Prostate;  
RX MEDLINE-98041505; PubMed-9375657;  
RA Bzdega T., Turz T., Wróblewska B., She D., Chung H.S., Kim H.,  
RA Neale J.H.;  
RT "Molecular cloning of a peptidase against N-acetylaspartylglutamate  
RT from a rat hippocampal cDNA library.";  
RL *J. Neurochem.* 69:2270-2277(1997).  
RN [4]  
RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM PSMA-1), AND VARIANT  
RP HIS-75.  
RX MEDLINE-99057588; PubMed-9838072; DOI-10.1016/S0167-4781(98)00200-0;  
RA O'Keefe D.S., Su S.L., Bacich D.J., Horiguchi Y., Luo Y., Powell C.T.,  
RA Zandvliet D., Russell P.W., Molloy P.L., Nowak N.J., Showe T.B.,  
RA Mullings C., Vonder Haar R.A., Fair W.R., Heston W.D.W.;  
RT "Mapping, genomic organization and promoter analysis of the human  
RT prostate-specific membrane antigen gene.";  
RL *Biochim. Biophys. Acta* 1443:113-127(1998).  
RN [5]  
RP NUCLEOTIDE SEQUENCE [mRNA] (ISOFORM PSMA-1).  
RC TISSUE=Brain;  
RX MEDLINE-98362085; PubMed-9694964;  
RA Luthi-Carter R., Barczak A.K., Speno H., Coyle J.T.;  
RT "Molecular characterization of human brain N-acetylated alpha-linked  
RT acidic dipeptidase (NAALADase).";  
RL *J. Pharmacol. Exp. Ther.* 286:1020-1025(1998).  
RN [6]  
RP NUCLEOTIDE SEQUENCE [mRNA] (ISOFORM PSMA-1), AND CHARACTERIZATION.  
RC TISSUE-Prostate;  
RX MEDLINE-99185063; PubMed-10085079; DOI-10.1074/jbc.274.13.8470;  
RA Pangalos M.N., Neef J.-M., Somer M., Verhasselt P., Bekkers M.,  
RA van der Helm L., Fraiponts E., Ashton D., Gordon R.D.;  
RT "Isolation and expression of novel human glutamate carboxypeptidases  
RT with N-acetylated alpha-linked acidic dipeptidase and dipeptidyl  
RT peptidase IV activity.";  
RL *J. Biol. Chem.* 274:8470-8483(1999).  
RN [7]  
RP NUCLEOTIDE SEQUENCE [mRNA] (ISOFORMS PSMA-1 AND PSMA-2), AND VARIANT  
RP TYR-475.  
RC TISSUE=Jejunum;  
RX PubMed-11092759; DOI-10.1093/hmg/9.19.2837;  
RA Devlin A.M., Ling E.-H., Pearson J.M., Fernando S., Clarke R.,  
RA Smith A.D., Halsted C.H.;  
RT "Glutamate carboxypeptidase II: a polymorphism associated with lower  
RT levels of serum folate and hyperhomocysteinemias.";  
RL *Hum. Mol. Genet.* 9:2837-2844(2000).  
RN [8]  
RP NUCLEOTIDE SEQUENCE [GENOMIC DNA] (ISOFORM PSMA-5).  
RA Peace D.J., Zhang Y., Holt G., Ferrer K.T., Heller M., Sosman J.A.,  
RA Xu B.H.;  
RT "Identification of three novel splice variants of prostate-specific  
RT membrane antigen.";  
RL Submitted (NOV-1998) to the EMBL/GenBank/DBJ databases.  
RN [9]  
RP NUCLEOTIDE SEQUENCE [mRNA], AND TISSUE SPECIFICITY.  
RC TISSUE-Liver;  
RX PubMed-14716746; DOI-10.1002/pros.10319;  
RA O'Keefe D.S., Bacich D.J., Heston W.D.W.;

RT "Comparative analysis of prostate-specific membrane antigen (PSMA) versus a prostate-specific membrane antigen-like gene.";  
RL Prostate 58:200-210(2004).  
RN [10]  
RP PARTIAL NUCLEOTIDE SEQUENCE [mRNA] (ISOFORMS PSMA-3 AND PSMA-4).  
RA Lupold S.E., Criley S.C., Coffey D.S.;  
RT "Alternative Splicing of the prostate-specific membrane antigen.";  
RL Submitted (APR 2000) to the EMBL/GenBank/DDBJ databases.  
RN [11]  
RP PROTEIN SEQUENCE OF 60-74, AND SUBCELLULAR LOCATION.  
RC TISSUE-Prostatic carcinoma;  
RX MEDLINE-99025849; PubMed-9809977;  
RA Grauer L.S., Lawler K.D., Marignac J.L., Kumar A., Goel A.S.,  
RA Wolfert R.L.;  
RT "Identification, purification, and subcellular localization of prostate-specific membrane antigen PSM' protein in the LNCaP prostatic carcinoma cell line";  
RL Cancer Res. 58:4787-4789(1998).  
RN [12]  
RP ALTERNATIVE SPLICING.  
RA Bzdega T., She D., Turi T., Wroblewska B., Neale J.H.;  
RT "Molecular cloning of alternatively spliced variants of the peptidase against N-acetylaspartylglutamate (NAAG) from human and rat nervous systems.";  
RL Abstr. - Soc. Neurosci. 24:579-579(1998).  
RN [13]  
RP CHARACTERIZATION.  
RX MEDLINE-96288196; PubMed-9622670; DOI=10.1016/S0006-8993(96)00244-3;  
RA Luthi-Carter R., Barczak A.K., Speno H.D., Coyle J.T.;  
RT "Hydrolysis of the neuropeptide N-acetylaspartylglutamate (NAAG) by cloned human glutamate carboxypeptidase II.";  
RL Brain Res. 795:341-348(1998).  
RN [14]  
RP DOMAIN STRUCTURE.  
RX MEDLINE-97330810; PubMed-9187245; DOI=10.1016/S0167-4838(97)00008-3;  
RA Rawlings N.D., Barrett A.J.;  
RT "Structure of membrane glutamate carboxypeptidase.";  
RL Biochim. Biophys. Acta 1339:247-252(1997).  
RN [15]  
RP MUTAGENESIS.  
RX MEDLINE-99102317; PubMed-9882712;  
RA Speno H.S., Luthi-Carter R., Macias W.L., Valentine S.L.,  
RA Joshi A.R.T., Coyle J.T.;  
RT "Site-directed mutagenesis of predicted active site residues in glutamate carboxypeptidase II.";  
RL Mol. Pharmacol. 55:179-185(1999).  
RN [16]  
RP GLYCOSYLATION AT ASN-76; ASN-336; ASN-459; ASN-476 AND ASN-638.  
RX MEDLINE-92660472; PubMed-12754519; DOI=10.1038/nbt827;  
RA Zhang H., Li X.-J., Martin D.B., Aebersold R.;  
RT "Identification and quantification of N-linked glycoproteins using hydrazide chemistry, stable isotope labeling and mass spectrometry.";  
RL Nat. Biotechnol. 21:660-666(2003).  
RN [17]  
RP GLYCOSYLATION AT ASN-51; ASN-76; ASN-121; ASN-140; ASN-153; ASN-195; ASN-336; ASN-459; ASN-476 AND ASN-638, AND MUTAGENESIS OF ASN-51; ASN-76; ASN-121; ASN-140; ASN-153; ASN-195; ASN-336; ASN-459; ASN-476; ASN-638 AND THR-640.  
RX PubMed-15152093; DOI=10.1110/ps.04622104;  
RA Barinka C., Sacha P., Sklenar J., Man P., Bezouska K., Slusher B.S.,  
RA Konvalinka J.;  
RT "Identification of the N-glycosylation sites on glutamate carboxypeptidase II necessary for proteolytic activity.";  
RL Protein Sci. 13:1627-1635(2004).  
CC !- FUNCTION: Has both folate hydrolase and N-acetylated-alpha-linked-acidic dipeptidase (NAALADase) activity. Has a preference for tri-alpha-glutamate peptides. In the intestine, required for the uptake of folate. In the brain, modulates excitatory neurotransmission through the hydrolysis of the neuropeptide, N-acetylaspartylglutamate (NAAG), thereby releasing glutamate. Isoforms PSM-4 and PSM-5 would appear to be physiologically

CC irrelevant. Involved in prostate tumor progression.  
 CC -!- FUNCTION: Also exhibits a peptidyl-peptidase IV type activity.  
 CC In vitro, cleaves Gly-Pro-AMC.  
 CC -!- CATALYTIC ACTIVITY: Release of an unsubstituted, C-terminal  
 CC glutamyl residue, typically from Ac-Asp-Glu or folylpoly-gamma-  
 CC glutamates.  
 CC -!- COFACTORs: Binds 2 zinc ions per subunit. Required for NAALADase  
 CC activity.  
 CC -!- ENZYME REGULATION: The NAALADase activity is inhibited by beta-  
 CC NAAG, quisqualic acid, 2-(phosphonomethyl) pentanedioic acid  
 CC (PMPA) and EDTA. Activated by cobalt.  
 CC -!- BIOPHYSICOCHEMICAL PROPERTIES:  
 CC pH dependence:  
 CC Stable at pH greater than 6.5;  
 CC -!- SUBCELLULAR LOCATION: Cell membrane; Single-pass type II membrane  
 CC protein. Isoform PSMA-5: Cytoplasm.  
 CC -!- ALTERNATIVE PRODUCTS:  
 CC Event-Alternative splicing; Named isoforms-6;  
 CC Comment-Experimental confirmation may be lacking for some  
 CC isoforms;  
 CC Name=PSMA-1;  
 CC      IsoId=Q04609-1; Sequence=Displayed;  
 CC Name=PSMA-2;  
 CC      IsoId=Q04609-2; Sequence=VSP\_005341;  
 CC Name=PSMA-3;  
 CC      IsoId=Q04609-3; Sequence=VSP\_005342;  
 CC Name=PSMA-4;  
 CC      IsoId=Q04609-4; Sequence=VSP\_005339, VSP\_005340;  
 CC Name=PSMA-5;  
 CC      IsoId=Q04609-5; Sequence=VSP\_005337, VSP\_005338;  
 CC Name=PSMA-6;  
 CC      IsoId=Q04609-6; Sequence=VSP\_005336;  
 CC -!- TISSUE SPECIFICITY: Highly expressed in prostate epithelium. Also  
 CC expressed, in the small intestine, brain, kidney, liver, spleen,  
 CC colon, trachea, spinal cord and the capillary endothelium of a  
 CC variety of tumors. Expressed specifically in jejunum brush border

Query Match 100.0%; Score 3983; DB 1; Length 750;  
 Best Local Similarity 100.0%; Pred. No. 1.6e-266;  
 Matches 750; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 MWNLHETDASAVATARPRMLCAGALVLAGGGFLLGLPFWIKSSNEATNITPKHNMK 60  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 1 MWNLHETDASAVATARPRMLCAGALVLAGGGFLLGLPFWIKSSNEATNITPKHNMK 60

Qy 61 FLDELKAENIKKFLYNTQIPIHLAGTEQNQFLAKQIQSQWKEFGLDSVELAHYDVLLS 120  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 61 FLDELKAENIKKFLYNTQIPIHLAGTEQNQFLAKQIQSQWKEFGLDSVELAHYDVLLS 120

Qy 121 NKTHPNYIISINEDGNEIFNTSLFEPPPPGYENVSIVPPFSAFSPQGMPEGDLVYNYA 180  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 121 NKTHPNYIISINEDGNEIFNTSLFEPPPPGYENVSIVPPFSAFSPQGMPEGDLVYNYA 180

Qy 181 RTEDEFFKLERDMKINCSKGKIVIARYGKVRGNKVKNAQLAGAKGVILYSDPADYFAPGVK 240  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 181 RTEDEFFKLERDMKINCSKGKIVIARYGKVRGNKVKNAQLAGAKGVILYSDPADYFAPGVK 240

Qy 241 SYPDGWNLGGGVQRGNILNLNGAGDPLTPGYPANEYAYRGLAEEAVGLPSIPVHPIGY 300  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 241 SYPDGWNLGGGVQRGNILNLNGAGDPLTPGYPANEYAYRGLAEEAVGLPSIPVHPIGY 300

Qy 301 DAQKLLEKMGGSAPPDSSWRGSLKVPYNNVPGPFTGNFSTQKVKMHIIHSTNEVTRIYNV 360  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 301 DAQKLLEKMGGSAPPDSSWRGSLKVPYNNVPGPFTGNFSTQKVKMHIIHSTNEVTRIYNV 360

Qy 361 TLRGAVEPDRYVILGGHRSWVPGIDPQSCAAVWHEIVRSFCTLKKEGMRPRTTILFAS 420  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||  
 Db 361 TLRGAVEPDRYVILGGHRSWVPGIDPQSCAAVWHEIVRSFCTLKKEGMRPRTTILFAS 420

Qy 421 WDAEEFGLGSTEWAZENSRLLQERGVAYINADSSIEGNYTLRVDCTPLMYSVLVHNLTK 480  
 ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| ||||| |||||

Db 421 WDAEFPGLGSTEWAENSRLLQERGVAYINADSSIEGNYTLRVDCPLMYSLVHNLTK 480  
Qy 481 LKSPDGEFEGKSLYESWTKSPSPFSGMPRISKLGSNDPEVFFQRLGIASGRARYTKN 540  
Db 481 LKSPDGEFEGKSLYESWTKSPSPFSGMPRISKLGSNDPEVFFQRLGIASGRARYTKN 540  
Qy 541 WETNKFGSPYPLYHSVYETYELVEKFYDPMFKYHLTVAQVRGGMWELANSIVLPFCDRDY 600  
Db 541 WETNKFGSPYPLYHSVYETYELVEKFYDPMFKYHLTVAQVRGGMWELANSIVLPFCDRDY 600  
Qy 601 AVVLRKYADKLYSISMKHPQEMKTYSVSFDSLFSAVKNFTEIAKFSERLQDFDKSNPIV 660  
Db 601 AVVLRKYADKLYSISMKHPQEMKTYSVSFDSLFSAVKNFTEIAKFSERLQDFDKSNPIV 660  
Qy 661 LRMNNDQIMFLERAFIGPLGLPDRPFYRVIYAPSSHNKYAGESFPGIYDALFDIESKVD 720  
Db 661 LRMNNDQIMFLERAFIGPLGLPDRPFYRVIYAPSSHNKYAGESFPGIYDALFDIESKVD 720  
Qy 721 PSKAWGEVKRQIYVAFTVQAAETLSEVA 750  
Db 721 PSKAWGEVKRQIYVAFTVQAAETLSEVA 750